

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
5 February 2004 (05.02.2004)

PCT

(10) International Publication Number  
**WO 2004/011630 A3**

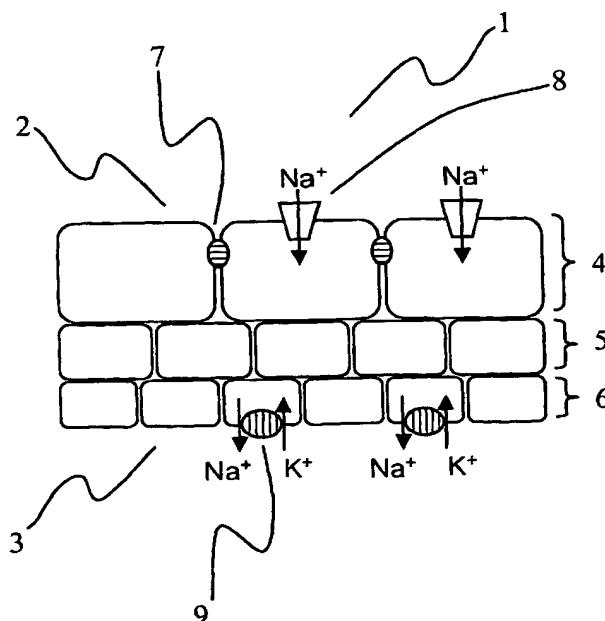
- (51) International Patent Classification<sup>7</sup>: **C12N 5/06** (74) Agent: **IP.21 LIMITED**; Norwich Research Park, Colney, Norwich NR4 7UT (GB).
- (21) International Application Number: **PCT/GB2003/003291** (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (22) International Filing Date: **28 July 2003 (28.07.2003)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
- (30) Priority Data: **0217314.4** **26 July 2002 (26.07.2002)** **GB** (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
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**Declarations under Rule 4.17:**

- *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii)) for the following designations AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES,*

[Continued on next page]

(54) Title: **BIOMIMETIC UROTHELIUM**



(57) Abstract: Urothelium is the specialised endothelium that lines much of the mammalian urinary tract. This invention relates to the field of *in vitro* urothelial culture. Previous methods produce tissue lacking much of the functionality of native urothelium. In this invention, stratified, differentiated mammalian urothelium (1) is produced by passing urothelial cells through a nutrient medium containing serum, and redispersed, before going on in a like medium to form said urothelium.



FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW, ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG)

— of inventorship (Rule 4.17(iv)) for US only

**Published:**

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

**(88) Date of publication of the international search report:**

29 April 2004

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

# INTERNATIONAL SEARCH REPORT

PCT/GB 03/03291

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 C12N5/06

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61L C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CROSS WILLIAM R ET AL: "The barrier function of in vitro generated human urothelium" JOURNAL OF UROLOGY, vol. 167, no. 4 Supplement, April 2002 (2002-04), page 32, XP0009025899 & ANNUAL MEETING OF THE AMERICAN UROLOGY ASSOCIATION, INC.; ORLANDO, FLORIDA, USA; MAY 25-30, 2002 ISSN: 0022-5347 abstract	1-3,5, 11,12
Y	----- -/--	6,8-10

☒ Further documents are listed in the continuation of box C.

☐ Patent family members are listed in annex.

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Date of the actual completion of the international search

13 February 2004

Date of mailing of the international search report

01/03/2004

Name and mailing address of the ISA

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## INTERNATIONAL SEARCH REPORT

PCT/GB 03/03291

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	CROSS W R ET AL: "The barrier properties of in vitro generated normal human urothelium" BIOCHEMICAL SOCIETY TRANSACTIONS, vol. 30, no. 1, 2002, page A44, XP0009025900 & 675TH MEETING OF THE BIOCHEMICAL SOCIETY JOINT WITH THE PHYSIOLOGICAL SOCIETY; YORK, ENGLAND, UK; DECEMBER 18-19, 2001 ISSN: 0300-5127 abstract	1-3, 5, 11, 12
X	TRUSCHEL STEVEN T ET AL: "Primary uroepithelial cultures: A model system to analyze umbrella cell barrier function" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 274, no. 21, 21 May 1999 (1999-05-21), pages 15020-15029, XP002270267 & ISSN: 0021-9258 the whole document	12
Y	LIEBERT MONICA ET AL: "Expression of mal is associated with urothelial differentiation in vitro: identification by differential display reverse-transcriptase polymerase chain reaction" DIFFERENTIATION, vol. 61, no. 3, 1997, pages 177-185, XP0009025896 & ISSN: 0301-4681 page 178, paragraph 3 page 180, paragraph 1 - page 181, left-hand column, paragraph 2 page 183, right-hand column, paragraph 1 page 184, right-hand column	6, 9
Y	SOUTHGATE J ET AL: "Normal human urothelial cells in vitro: proliferation and induction of stratification." LABORATORY INVESTIGATION; A JOURNAL OF TECHNICAL METHODS AND PATHOLOGY. OCT 1994, vol. 71, no. 4, October 1994 (1994-10), pages 583-594, XP0009025904 ISSN: 0023-6837 the whole document	10

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## INTERNATIONAL SEARCH REPORT

PCT/GB 03/03291

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KREFT MATEJA ERDANI ET AL: "Antigenic and ultrastructural markers associated with urothelial cytodifferentiation in primary explant outgrowths of mouse bladder" CELL BIOLOGY INTERNATIONAL, vol. 26, no. 1, 2002, pages 63-74, XP002270270 & ISSN: 1065-6995 the whole document	8
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A	SUGASI SITA ET AL: "In vitro engineering of human stratified urothelium: Analysis of its morphology and function" JOURNAL OF UROLOGY, vol. 164, no. 3 Part 2 of 2, September 2000 (2000-09), pages 951-957, XP0009025878 & ISSN: 0022-5347 the whole document	
A	LUDWIKOWSKI B ET AL: "The long-term culture of porcine urothelial cells and induction of urothelial stratification" BJU INTERNATIONAL, vol. 84, no. 4, September 1999 (1999-09), pages 507-514, XP002270273 & ISSN: 1464-4096 page 508	
A	PARIENTE J L ET AL: "Cultured differentiated human urothelial cells in the biomaterials field" BIOMATERIALS, vol. 21, no. 8, April 2000 (2000-04), pages 835-839, XP002270274 & ISSN: 0142-9612 the whole document	